

WHAT IS CLAIMED IS:

1. An *in vivo* method of therapeutic or prophylactic genetic immunization of a mammalian host, which comprises:

(a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;

(b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;

(c) inoculating said mammalian host with said particulate polynucleotide; and,

(d) delivering said particulate polynucleotide to the cytoplasm of a target cell within said mammalian host, such that said expressed antigenic protein or antigenic protein fragment is presented to the membrane surface of said target cell through the MHC class I pathway.

2. The method of claim 1 wherein said mammalian host is a human.

3. The method of claim 2 wherein said DNA fragment expresses a tumor rejection antigen, viral antigen or antigenic protein fragment thereof.

4. The method of claim 3 wherein said target cell is an antigen presenting cell.

5. The method of claim 4 wherein said antigen presenting cell resides within or migrates to the lymphoid tissue of said human host.

6. The method of claim 5 wherein said tumor rejection antigen is selected from the group consisting of MAGE-1 and MAGE 3.

7. The method of claim 5 wherein said tumor rejection antigen is Melan-A.

8. The method of claim 5 wherein said tumor rejection antigen is gp100.

9. The method of claim 5 wherein said tumor rejection antigen is p53.

10. The method of claim 5 wherein said tumor rejection antigen is CEA.

11. The method of claim 5 wherein said tumor rejection antigen is HER2/neu.

12. The method of claim 5 wherein said viral antigen is HIV gp120, HIV gp160.

13. The method of claim 5 wherein said viral antigen is Influenza virus nucleoprotein.

14. The method of claim 5 wherein said viral antigen is Hepatitis B surface antigen.

15. An *in vivo* method of therapeutic or prophylactic genetic immunization of a mammalian host, which comprises:

- 5
- (a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;
 - (b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;
 - (c) inoculating said mammalian host with said particulate polynucleotide using a biolistic device; and,
 - (d) delivering said particulate polynucleotide to the cytoplasm of a target cell within said mammalian host, such that said expressed antigenic protein or antigenic protein fragment is presented to the membrane surface of said target cell through the

~~MHC class I pathway.~~

16. The method of claim 15 wherein said mammalian host is a human.

17. The method of claim 16 wherein said DNA fragment expresses a tumor rejection antigen, viral antigen or antigenic protein fragment thereof.

18. The method of claim 17 wherein said target cell is an antigen presenting ~~cell.~~

19. The method of claim 18 wherein said antigen presenting cell resides within or migrates to the lymphoid tissue of said human host.

20. The method of claim 19 wherein said tumor rejection antigen is selected from the group consisting of MAGE-1 and MAGE 3.

21. The method of claim 19 wherein said tumor rejection antigen is Melan-A.

22. The method of claim 19 wherein said tumor rejection antigen is gp100.

23. The method of claim 19 wherein said tumor rejection antigen is p53.

24. The method of claim 19 wherein said tumor rejection antigen is CEA.

25. The method of claim 19 wherein said tumor rejection antigen is HER2/neu.

26. The method of claim 19 wherein said viral antigen is HIV gp120, HIV gp160.

27. The method of claim 19 wherein said viral antigen is Influenza virus nucleoprotein.

28. The method of claim 19 wherein said viral antigen is Hepatitis B surface antigen.

29. An *in vivo* method of therapeutic or prophylactic genetic immunization of a mammalian host, which comprises:

- Sub E1
- 5 (a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;
- (b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;
- (c) inoculating said mammalian host with said particulate polynucleotide by direct injection; and,
- 10 (d) delivering said particulate polynucleotide to the cytoplasm of a target cell within said mammalian host, such that said expressed antigenic protein or antigenic protein fragment is presented to the membrane surface of said target cell through the ~~MHC class I pathway.~~

30. The method of claim 29 wherein said mammalian host is a human.

15 31. The method of claim 30 wherein direct injection is by subcutaneous injection.

Sub E1) 32. The method of claim 31 wherein said recombinant DNA vector fragment expresses a tumor rejection antigen, viral antigen or antigenic protein fragment thereof.

~~33. The method of claim 32 wherein said target cell is an antigen presenting cell.~~

20 34. The method of claim ³²~~33~~ wherein said antigen presenting cell resides within or migrates to the lymphoid tissue of said human host.

35. The method of claim 34 wherein said tumor rejection antigen is selected from the group consisting of MAGE-1 and MAGE 3.

36. The method of claim 34 wherein said tumor rejection antigen is Melan-A.

25 37. The method of claim 34 wherein said tumor rejection antigen is gp100.

38. The method of claim 34 wherein said tumor rejection antigen is p53.

39. The method of claim 34 wherein said tumor rejection antigen is CEA.

40. The method of claim 34 wherein said tumor rejection antigen is HER2/neu.

30 41. The method of claim 34 wherein said viral antigen is HIV gp120, HIV gp160.

42. The method of claim 34 wherein said viral antigen is Influenza virus nucleoprotein.

43. The method of claim 34 wherein said viral antigen is Hepatitis B surface antigen.

44. An *ex vivo* method of therapeutic or prophylactic genetic immunization of a mammalian host, which comprises:

(a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;

(b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;

(c) delivering said particulate polynucleotide to the cytoplasm of a target cell of a mammalian host *in vitro*, such that said expressed antigenic protein or antigenic protein fragment is presented on the membrane surface of said target cell through the MHC class I pathway; and,

(d) inoculating said mammalian host with said target cell by direct injection

45. The method of claim 44 wherein said mammalian host is a human.

46. The method of claim 45 wherein direct injection is by subcutaneous injection.

47. The method of claim 46 wherein said recombinant DNA vector fragment expresses a tumor rejection antigen, viral antigen or antigenic protein fragment thereof.

48. The method of claim 47 wherein said target cell is an antigen-presenting cell.

49. The method of claim 48 wherein said antigen presenting cells resides within or migrates to the lymphoid tissue of said human host.

50. The method of claim 49 wherein said tumor rejection antigen selected from the group consisting of MAGE-1 and MAGE 3.

51. The method of claim 49 wherein said tumor rejection antigen is Melan-A.

52. The method of claim 49 wherein said tumor rejection antigen is gp100.

53. The method of claim 49 wherein said tumor rejection antigen is p53.

54. The method of claim 49 wherein said tumor rejection antigen is CEA.

55. The method of claim 49 wherein said tumor rejection antigen is HER2/nue.

56. The method of claim 49 wherein said viral antigen is HIV gp120, HIV gp160.

57. The method of claim 49 wherein said viral antigen is Influenza virus nucleoprotein.

58. The method of claim 49 wherein said viral antigen is Hepatitis B surface antigen.

59. An *ex vivo* method of therapeutic or prophylactic genetic immunization of a mammalian host, which comprises:

(a) generating a DNA fragment(s) which express a molecule which enhances the antigen presentation function of an APC;

(b) distributing said DNA fragment(s) on a particle surface, resulting in a particulate polynucleotide;

(c) delivering said particulate polynucleotide to the cytoplasm of a target cell of a mammalian host *in vitro*, such that said expressed antigen presentation enhancing protein or proteins is expressed in a biologically significant form and at biologically significant levels;

(d) inoculating said mammalian host with said target cell by direct injection.

60. The method of claim 59 wherein said mammalian host is a human.

61. The method of claim 60 wherein direct injection is by subcutaneous injection.

~~62. The method of claim 61 wherein said target cell is an antigen presenting cell.~~

63. The method of claim ⁶¹~~62~~ wherein said antigen presenting cell resides within or migrates to the lymphoid tissue of said human host.

64. The method of claim 63 wherein said DNA vector fragment expresses a costimulatory molecule.

65. The method of claim 64 wherein said costimulatory molecule is selected from the group consisting of CD80 and CD86.

66. The method of claim 63 wherein said DNA vector fragment expresses a cytokine molecule.

67. The method of claim 66 wherein said cytokine molecule is selected from the group consisting of IL-12, IL-4 and IL-2.